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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Umberto Benatti

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EXAMINER

NIEBAUER, RONALD T

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/584,874	Applicant(s) BENATTI ET AL.	
	Examiner RONALD T. NIEBAUER	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 March 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-28 is/are pending in the application.
- 4a) Of the above claim(s) 19-22 and 24-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-18 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/8/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 15-18,23) and the species where R is H (see claim 16) in the reply filed on 3/12/08 is acknowledged. The traversal is on the ground(s) that the claims share a common special technical feature which is the novel glutathione derivatives recited in claim 15. Applicants argue that Anderson et al. (US 5,464,825) teach derivatives in which the glycine carboxyl group is esterified while the instant claims have a free carboxyl group. Applicants argue that the International Search Report is evidence of unity of invention. Applicants argue that the groups have not been identified as being in the same class and no evidence exists that there would be a serious burden on the examiner.

Applicants argument is not found persuasive. It is noted that applicant has stated that (page 2 last paragraph) that there may be a lack of unity if a common technical feature is obvious. As discussed in detail below, Anderson and McMurry render instant claim 15 unpatentable. Briefly, Anderson teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). Anderson teach that the compounds are hydrolyzed (column 4 line 21) to form N-acyl GSH which is the de-esterified compound. Thus, N-acyl GSH (where R is propyl) meets the limitations of claim 15 as currently interpreted. Thus the common technical feature does not make a contribution over the prior art.

Although applicants argue that the International Search Report is evidence of unity of invention, Anderson and McMurry (as discussed in detail below) show otherwise.

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Although applicants argue that there is no burden. There is burden for one or more of the following reasons: the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries); the prior art applicable to one invention would not likely be applicable to another invention; the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph. Further it is noted that claim 1 is drawn to compounds where R is a thiol protection group. Thiol protection group represents a genus. A search when R is H would not necessarily uncover art when R is acetyl for example. It is noted that each of groups 2-5 as set forth previously represents specific diseases. As such, art on one specific disease would not necessarily teach a different disease. Further, art that teaches a compound would not necessarily teach steps of administration.

The requirement is still deemed proper and is therefore made FINAL.

Applicant states (page 5 of reply) that claims readable on the elected species are 15-18,23.

Claims 19-22,24-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/12/08.

Claims 1-14 have been cancelled.

Claims 15-18,23 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) was submitted on 6/8/07. The information disclosure statement has been considered by the examiner. It is noted that JP-57134410 and JP-63002922 include abstracts in the English language.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-18,23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites 'the medicament of claim 18'. As such the claims refers to itself and it is unclear which claim it is intended to depend from.

Claim 15 shows a formula in which the first residue (position of glycine in non-derivatized form) has no carboxyl group. However, Figure 1 shows a structure with the first residue having a carboxyl group. Applicants state (page 2 of reply) that the structure should properly be the structure set forth in Figure 1. However, no such change has been made in the claims. Further, Figure 1 does not include an R variable as in instant claim 15. As such, the scope of claim 15 and dependent claims 16-18,23 is unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-18,23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 5,464,825 as cited previously) and McMurry (Organic Chemistry 4th edition 1996, page 825).

Anderson teach methods for increasing glutathione (GSH) levels or levels of glutathione equivalents (column 3 lines 22-23). Anderson specifically recites N-acyl glutathiones as a type of glutathione derivative (column 3 line 24). Anderson teaches that the acyl group can contain 1 to 9 carbon atoms and is preferably 1 to 4 carbon atoms, for example propyl (column 3 lines 33-37). Anderson teach that acylated esters are de-esterified in the cell (column 3 line 29,67).

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Anderson teach that elevated GSH levels are desired in the treatment of viral infections (column 3 lines 11-18).

Anderson specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson specifically teach that the R1 is preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). Anderson teach that the compounds are hydrolyzed (column 4 line 21) to form N-acyl GSH which is the de-esterified compound. Anderson teach pharmaceuticals of such compounds (column 4 lines 30-32). Anderson does not expressly show the reaction scheme of the hydrolysis reaction. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson (column 4 line 21) includes a carboxylic acid not an ester.

Neither of the references expressly teach the compound of the instant invention.

Anderson specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. When R1 is propyl and the compound is de-esterified (column 3 line 29,67) or hydrolyzed (column 4 line 21) as described by Anderson the resulting product is a carboxylic acid that is identical to the compound of claim 16 of the instant invention where R is H (the elected species). Thus the limitations of claims 15-16 as currently interpreted are met.

In other words, the disclosure of 'N-acyl GSH' (column 4 line 21) includes various compounds that have been hydrolyzed. Since Anderson teach such compounds as pharmaceuticals (column 4 line 30-32), teach carriers (column 5 lines 23-30) and teach applications for treatment of viral infections (column 2 line 11-18) the limitations of claims 17-18,23 are met.

It is noted that the applicants have provided contradictory statements regarding the claimed invention (see 112 2nd). Since the applicants state (page 2 of reply) that the proper structure is the structure set forth in Figure 1 (not the structure as set forth in claim 15), for purposes of examination claim 15 has been interpreted as being drawn to the compound as shown in Figure 1 (has a carboxyl group on the glycine residue) with SR instead of SH. Claim 18 (see 112 2nd) has been treated as if it limits claim 17.

It has been recently held that "obvious to try" may be an appropriate test under 103 KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The Supreme Court stated in *KSR*

When there is motivation

"to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the claims would have been obvious because 'a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense'. In particular, Anderson recognize the need for increasing GSH cellular levels

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(column 2-3) and teach a finite number of compounds to be used (column 4 line 10-30). Further, Anderson specifically teach R1 values and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that the compound with R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. Further, such compounds are described as being de-esterified and hydrolyzed. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Response to Arguments Lack of unity

It is noted that this is the first office action on the merits. Since applicants have provided arguments regarding the Anderson patent which is used in the instant rejection such arguments will be addressed.

Applicants argue that Anderson teach derivatives in which the glycine carboxyl group is esterified while the instant claims have a free carboxyl group

Applicant's arguments filed 3/12/08 have been fully considered but they are not persuasive.

In addition to the esters, Anderson teach that compounds are de-esterified (column 3 line 29,67) and hydrolyzed (column 4 line 21) As discussed above, Anderson teach N-acyl GSH (column 4 line 21). As discussed above, McMurry clearly set forth that carboxylic acids are products of hydrolysis, in fact the section of McMurry is named 'Hydrolysis: Conversion of

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Esters into Carboxylic Acids'. As such, Anderson teach compounds in which the glycine residue has a free carboxyl group.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/
Examiner, Art Unit 1654

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